

CLAIMS

What is claimed is:

1. A method for the treatment or alleviation of depression or other affective disorders comprising administering an amount of an anti-inflammatory agent effective to treat or alleviate depression or other affective disorder to a subject in need thereof.

2. The method of claim 1, wherein said anti-inflammatory agent down-regulates peripheral cytokine levels to thereby treat or alleviate depression or other affective disorder.

3. The method of claim 2, wherein said anti-inflammatory agent acts peripherally to modulate the hypothalamic-pituitary-adrenal (HPA) axis to thereby treat or alleviate depression or other affective disorder.

4. The method of claim 1 wherein said anti-inflammatory agent comprises a compound selected from the group consisting of a non-steroidal anti-inflammatory drug (NSAID), a disease modifying antirheumatic drug (DMRAD), a statin and a macrolide antibiotic.

5. The method of claim 4, wherein said NSAID is selected from the group consisting of salicylates, arylpropionic acids, anthranilic acids, pyrazoles, cyclic acetic acids oxicams and selective Cox2 inhibitors.

6. The method of claim 4 in wherein said NSAID is an R-enantiomer of said NSAID.

7. The method of claim 6 in which said R-enantiomer of said NSAID is selected from a group consisting of R-ketoprofen, R-flurbiprofen, R-naproxen, R-

tiaprofenic, R-etodolac, R-ketorolac, R-suprofen, R-carprofen, R-pirprofen, R-indoprofen, R-benoxaprofen, R-ibuprofen.

8. The method of claim 6 wherein the ratio of said R-enantiomer NSAID to a S-enantiomer NSAID is at least 90:10 by weight.

9. The method of claim 8 wherein the ratio is at least 99:1 by weight.

10. The method of claim 4, wherein said anti-inflammatory agent comprises an agent selected from the group consisting of sulindac, diclofenac, tenoxicam, ketorolac, naproxen, nabumetone, diflunasal, ketoprofen, arlypropionic acids, tenidap, hydroxychloroquine, sulfasalazine, celecoxib, rofecoxib, meloxicam, etoricoxib, valdecoxib, methotrexate, etanercept, infliximab, adalimumab, or atorvastatin, fluvastatin, lovastatin, pravastatin, simvastatin clarithromycin, azithromycin, roxithromycin, erythromycin ibuprofen, dexibuprofen, flurbiprofen, fenoprofen, fenbufen, benoxaprofen, dexketoprofen, tolfenamic acid, nimesulide and oxaprozin.

11. The method of claim 1 wherein said antidepressant agent comprises an agent selected from the group consisting of imipramine, amitriptyline, desipramine, chloroimipramine, dibenzepin, doxepin, dosulepin, maprotilene, nortriptylene, mianserin, trimipramine, trazadone, nefazadone, mirtazapine, reboxetine, tranlycypromine, moclobemide, brofaramine, paroxetine, fluoxetine, sertraline, fluvoxamine, citalopram, escitalopram, venlafaxine, duloxetine, buspirone, flibanserin, bupropion and modafinil.

12. The method of claim 1, wherein said depression is selected from the group consisting of major depressive disorder, dysthymic disorder, bipolar I disorder, bipolar II disorder, cyclothymic disorder and drug-induced depression.

13. The method of claim 1 wherein said subject in need is refractory to antidepressant agents, suffering from melancholic depression or both.

14. The method of claim 1 wherein said subject in need has a pre-existing cardiac or vascular disease.

15. The method of claim 14, wherein said cardiac or vascular disease is selected from the group consisting of coronary artery disease, angina, and hypertension.

16. A method for the treatment of depression or other affective disorder comprising administering an effective amount of an anti-inflammatory agent to a subject in need thereof, wherein said anti-inflammatory agent down-regulates peripheral serum levels of a pro-inflammatory molecule or up-regulates peripheral serum levels of an anti-inflammatory molecule or both.

17. The method of claim 16, wherein said pro-inflammatory molecule is selected from the group consisting of interleukin-1, interleukin-6, interferon-gamma, TFN-alpha, and an activator of the interleukin-6 receptor.

18. The method of claim 16, wherein said anti-inflammatory molecule is interleukin-10.

19. A method for potentiating the action of an antidepressant agent comprising administering an effective amount of a combination of agents to a subject in need thereof, wherein said combination comprises an effective amount an antidepressant agent and an amount of an anti-inflammatory agent effective to treat or alleviate depression or other affective disorder.

20. The method of claim 19 wherein said antidepressant agent and said anti-inflammatory agent are formulated into a single pharmaceutical product.

21. The method of claim 19 wherein said antidepressant agent and said anti-inflammatory agent are provided in separate doses in a patient pack wherein said patient pack includes an explanatory leaflet for use by the subject.

22. The method of claim 19 in which the antidepressant agent employed is fluoxetine, whereby administration of said antidepressant agent inhibits the metabolism of the anti-inflammatory drug.

23. A method for the treatment or prevention of drug induced depression comprising administering an amount of an anti-inflammatory agent effective to treat or alleviate depression to a subject in need thereof.

24. The method of claim 23, wherein said drug-induced depression is induced by treatment with interferons or interleukins.

25. The method of claim 24, wherein said interferons are selected from the group consisting of interferon-1a and interferon 1-b.

26. The method of claim 24 wherein a combination of agents is used comprising an effective dose of an antidepressant agent and an amount of an anti-inflammatory effective in the treatment or alleviation of depression or other affective disorder.

27. The method of claim 26, wherein said antidepressant is selected from the group consisting of interferon alpha and interferon beta.

28. The method of claim 26, wherein said anti-inflammatory is selected from the group consisting of a NSAID, a DMARD, a statin and a macrolide antibiotic.

29. The method of claim 26 wherein said antidepressant and said anti-inflammatory are formulated into a single pharmaceutical composition.

30. The method of claim 26 wherein said antidepressant and said anti-inflammatory are supplied separately in a patient pack, wherein said patient pack further comprises an information leaflet for use by the subject.

31. A method for the identification of an anti-inflammatory agent for use in the treatment of depression and affective disorders which comprises:

- (a) inducing pro-inflammatory cytokines in a test animal;
- (b) administering a test agent to the test animal;
- (c) obtaining a blood sample from the test animal;
- (d) assaying the blood sample;
- (e) determining the levels of IL-1, IL-6 and TNF in said blood; and
- (f) identifying a compound that down regulates pro-inflammatory cytokine production.

32. The method of claim 31, further comprising the step:

- (g) selecting from this group of candidate agents based on tolerability in humans.

33. The method of claim 31, wherein said test animal is a rodent.

34. The method of claim 31, wherein said inducing step comprises inducing pro-inflammatory cytokines by injecting LPS.

35. The method of claim 31, wherein said inflammatory cytokine is IL-6.